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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,669	01/24/2002	Ibert C. Wells	N1427-005	1066

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EXAMINER	
SZPERKA, MICHAEL EDWARD	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/053,669	WELLS, IBERT C.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 24-31* is/are pending in the application.

4a) Of the above claim(s) *24-27 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,28,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/13/04, 3/7/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

1. *Claims 1, 2, and 24 have been amended.*

Claims 11-23 have been cancelled.

Claims 29-31 have been added.

Claims 1-10 and 24-31 are pending in the instant application.

Claims 24-27 stand withdrawn as per the Office action mailed October 4, 2004.

Newly submitted claim 29 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the antibodies of the elected invention can be made by techniques such as phage-display, rather than the recited method of hybridoma production.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 29 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-10, 28, and 30-31 are under examination in this Office Action.

Applicant is reminded to update the first line of the specification to indicate that application 09/265,690 has issued as US Patent No. 6,372,440.

Response to Arguments

2. Applicant has traversed the withdrawal of claims 24-27 in the response received February 4, 2005. The restriction request was made final for the reasons of record in the Office action mailed October 4, 2004, and at that time all claims drawn to non-elected inventions were withdrawn. Applicant is reminded that process claims that are commensurate in scope with an allowed product claim will be rejoined as a matter of right at the time of allowance. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

4. Claims 1, 2, 7-10 and 28 stand rejected and new claims 30 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody that specifically binds the sequence of SEQ ID NO: 1 and SEQ ID NO: 4 does not reasonably provide enablement for an antibody that specifically binds SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention

commensurate in scope with these claims for the reasons of record set forth in the office action mailed October 4, 2004.

Applicant has argued on pages 6-10 of the response received on February 4, 2005, that the specification is enabled for antibodies that specifically bind a sequence consisting of the four amino acid sequence FGLM (SEQ ID NO:2). Applicant argues that the fact that Couraud et al. (of record) failed to find either polyclonal or monoclonal antibodies that bound a peptide consisting of SEQ ID NO:2 is not surprising. Applicant's arguments have been considered, but they are not persuasive.

Applicant first argues that the art of Dery et al. and Frickey et al., cited by Applicant on pages 6-8 of the response received February 4, 2005, indicate that different regions of SP are important for generating antibody responses, and that the choice of a carrier protein to make conjugates influences the identity of the SP residues recognized by the antibodies. However, these arguments are not pertinent since the critical issue is the specific recognition of a peptide that is only 4 amino acids long, and neither reference cited by Applicant demonstrates the specific recognition of a peptide only 4 amino acids long from anywhere within the 11 residue sequence of SP since said references simply mutate positions of larger peptides to monitor the effect on binding (Dery et al.) or make truncations (Frickey et al.). Both Table I of Dery et al. (page 70, the peptide of SEQ ID NO:2) and Figure 1 of Frickey et al. (page 689, amino acids 1-4 of SP) indicate the failure of 4 amino acid peptides to bind the antibodies generated by these investigators even though the same antibodies do bind SP sequences of 5 or more residues.

Applicant then argues in the second paragraph of page 8 of the response that Couraud et al. failed to find an antibody that binds a peptide consisting of SEQ ID NO:2 because the antibodies generated by Couraud et al. were obtained by immunizing mice with the full length 11 amino acid sequence of substance P (SP) and the SP fragment identified as SEQ ID NO:2 lacks the conformational epitope of the intact peptide. However, the prior art clearly chows that the antibodies of Couraud et al. do bind fragments, specifically peptides consisting of SEQ ID NOs:1 and 4 (see particularly Table 3 on page 1714). As such, fragments maintain the native conformational epitope.

Applicant's final argument on pages 8-10 is that only routine experimentation would be required to generate an antibody of the requisite specificity, and that the examiner has provided no other reference other than Couraud et al. to demonstrate that the claimed invention is not fully enabled for antibodies that bind a peptide consisting of SEQ ID NO:2. This second argument has also been considered but has not been found persuasive.

As a rebuttal to Applicant's arguments that the teachings of Couraud et al. fail to indicate that greater than routine experimentation would be required to generate an antibody that binds to a peptide consisting of SEQ ID NO:2, Applicant is invited to consider the teachings of Harlow et al. (Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory, 1988, cited by applicant on page 15, paragraph 46 of the instant specification). Harlow et al. teach that the smallest synthetic peptide that will consistently elicit an antibody responses is 6 amino acids in length, and they recommend that peptides of approximately 10 residues should generally be used as a

lower limit for the production of antibodies (see Harlow et al., Antibodies, Chapter 5, page 76). As such, the generation of an antibody that binds an epitope of 4 amino acids is not considered a routine procedure that is generally performed in the art.

Therefore, based upon the teachings of Couraud et al., it does not appear that an antibody that specifically binds a sequence consisting of SEQ ID NO: 2 can be made using standard art recognized techniques, but antibodies that specifically bind a sequence consisting of SEQ ID NO: 1 or 4 can be successfully produced as was demonstrated by Couraud et al. Applicant has not disclosed that an antibody that specifically binds a sequence consisting of SEQ ID NO: 2 has been made, nor has Applicant indicated any additional techniques in addition to those commonly known in the art that would be required to overcome the difficulty in generating an antibody that specifically binds a sequence consisting of SEQ ID NO: 2. Applicant is reminded that argument does not replace evidence where evidence is necessary. See MPEP 2145. The scope of the claims must bear a reasonable correlation with the scope of enablement set forth, and without additional guidance, it is not possible to practice the full breadth of Applicant's claims as an undue amount of experimentation would be required to make an antibody that specifically binds a sequence consisting of SEQ ID NO: 2.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The rejection of claims 1-10 and 28 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter has been withdrawn due to Applicant's amendment to indicate that the claimed antibodies are isolated.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 9-10, and 28 stand rejected and new claim 30 is rejected under 35 U.S.C. 102(b) as being anticipated by Couraud et al. (J. Neurochemistry, 1987, 49:1708-1718, of record, see entire document) for the reasons of record as set forth in the Office action mailed October 4, 2004.

Applicant has argued on pages 10 and 11 of the response received February 4, 2005, that the rejection should be removed due to Applicant's amendment of the claims to recite antibodies that are "raised against" the recited SEQ ID numbers. As such, applicant is arguing a product by process limitation wherein since the prior art

antibodies were not made in the claimed manner, the prior art antibodies cannot have the same properties. Specifically, since the antibodies disclosed by Couraud et al. were raised against the intact eleven amino acid SP peptide sequence (Applicant's recited SEQ ID numbers are fragments of the SP peptide), Applicant argues that the claimed antibodies raised against SEQ ID NOs: 1, 2, or 4 are free of the prior art. This argument has been considered but is not persuasive because the prior art antibodies of Couraud et al. have the same properties regardless of how they were made.

Couraud et al. teach the generation of a polyclonal serum and monoclonal antibodies that specifically bind the recited sequences and the use of such antibodies as diagnostic reagents (see Table 3 on page 1714). Couraud et al also teach the hybridoma cell lines that secrete the monoclonal antibodies of the requisite specificity (see particularly the section titled Production and purification of mAbs on page 1709). Applicant's amendment to the claims only indicated how the antibody was made, but how the antibody was generated does not alter the structure or the antigen binding specificity of the recited antibody. As such, the newly recited limitation does not obviate the fact that the binding specificities of the antibodies and hybridomas disclosed by Couraud et al. anticipate the claimed invention and thus the antibodies of Couraud et al. meet the structural limitations of the claimed products.

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is

unpatentable even though the prior product was made by a different process." See MPEP 2113.

7. The following new ground of rejection is necessitated by Applicant's amendment filed February 4, 2005.

8. Claim 31 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has added new claim 31, and has indicated on pages 5 and 6 of the response received February 4, 2005 where support for the limitation "wherein the antibody has no significant reactivity to tachykinins of mammalian origin". Upon a review of the specification with particular attention paid to paragraphs indicated by Applicant as providing support for the new limitation, the examiner has been unable to locate either verbatim or implicit support for the new claim language. As such, the claim appears to contain new matter not disclosed at the time the instant application was filed. Applicant is required to either remove the new matter or specifically point out where support for the limitation "wherein the antibody has no significant reactivity to tachykinins of mammalian origin" can be found in either the specification or claims as originally filed.

9. No claims are allowable.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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